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Aripiprazole and valproate combination for chronic schizophrenia with dental treatment: a case report

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To the Editor: Patients with schizophrenia often have extensively untreated dental disease [1] and a very recent meta-analysis [2] of 8 studies comprising 2640 patients with schizophrenia and 19,698 healthy controls showed that the patients with schizophrenia had significantly higher scores of dental caries, missing teeth, and decayed teeth compared to controls while the schizophrenia patients had fewer score of filled teeth than the controls, indicating decreased access to dental care. We report herewith a patient with chronic schizophrenia, responding to aripiprazole and valproate combination and successfully receiving dental treatment without psychotic exacerbation. We obtained a signed informed consent from the patient for the publication of this case report.

Case report: A 63-year-old man, diagnosed as suffering from schizophrenia according to DSM-5, was admitted to a psychiatric ward at the university hospital, and his delusion of persecution and tantrum were improved after treatment with 4 mg/day of risperidone and 500 mg/day of carbamazepine. In addition, because the patient had many dental caries, he was treated by a dentist, although the patient also disliked dental treatment. His delusion was soon exacerbated because of bleeding after dental treatment; subsequently, he developed excitement and violence, and he was consequently secluded in an isolation room in the psychiatric ward. He gradually responded to 5 mg/day of risperidone and 900 mg/day of carbamazepine. Two months after discharge from the isolation room, he was transferred to a psychiatric hospital.

After admission to the psychiatric hospital, the patient gradually showed catatonia; therefore, he was restrained in the bed. The clinical syndrome gradually improved after treatment where risperidone was changed to paliperidone, olanzapine, and finally aripiprazole, and he was stable with 24 mg/day of aripiprazole and 600 mg/day of valproate. After the restraint was removed, the dosage form was changed to aripiprazole long-acting injection (LAI) (400 mg/month). Subsequently, because of the remaining dental caries, he was treated by the same dentist, who was working mainly at the university hospital and weekly at the psychiatric hospital. Surprisingly, his delusion was not exacerbated by the bleeding after the treatment. After 1 year of follow-up, he continued to receive 400 mg/month of LAI, 600 mg/day of valproate, and 50 mg/day of quetiapine.

In this case, two dental treatments were performed in the university hospital and in the psychiatric hospital, respectively. The dentist was the same one, and both dental treatments were similar; therefore, different responses of the patient were not because of the dental treatment effects. Instead, the difference in the pharmacotherapy might have been responsible for the different responses. It seems likely that the combination of aripiprazole and valproate is better for improving the psychotic exacerbation

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triggered by dental treatment than that of risperidone and carbamazepine.

From the viewpoints of pharmacokinetics, coadministration with valproate decreased the area under the curve and the maximum concentration of aripiprazole only by 24% and 26%, respectively, with minimal effects on the active metabolite [3]. However, the sum of the concentrations of risperidone and 9-OH-risperidone was significantly lower in patients receiving carbamazepine coadministration (median concentration, 44 nmol/L) than in those treated with risperidone alone (150 nmol/L) [4]. The results suggest that carbamazepine markedly decreases the plasma concentrations of risperidone and its active 9-OH-metabolite probably by inducing CYP3A4-mediated metabolism, and valproate does not cause any major changes in plasma aripiprazole levels.

In this case, it seems probable that the combination of aripiprazole and valproate, with LAI as a dosage form that avoids non-compliance, might help to maintain plasma aripiprazole levels, although the levels were not actually measured. Probably, the maintained aripiprazole levels may contribute to prevention of exacerbation triggered by the second dental treatment or subsequent other stressful events that occurred in the patient.

Conflict of interest

Takeshi Terao received lecture fees from Otsuka pharmaceutical company. The other authors had no conflict of interest.

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